Remarks

Claims 1-21, 24, 34, 39, and 41-51 have been cancelled without disclaimer of or prejudice to the underlying subject matter. New claims 52-56 have been added. This application presently contains claims 22, 23, 25-33, 35-38, 40, and 52-56. No new matter is added by these amendments. Support for these amendments may be found in the original claims, the sequence listing, the figures, and throughout the specification, *e.g.*, at page 17, line 10 through page 18, line 12; page 48, line 12 through page 53, line 6; page 103, line 18 through page 105, line 20; Examples 1 and 2; and Tables 1 and 4. Applicants respectfully request entry of the foregoing amendments and submit that these amendments put the application in condition for immediate allowance or appeal.

A. The Restriction Requirement

Applicants acknowledge the finality of the restriction requirement but maintain their traversal on the grounds that the Examiner has not shown that a search and examination of the entire application would cause a serious burden. Applicants also submit that the Examiner has failed to meet her burden to provide an example to satisfy M.P.E.P. § 806.05(h), pages 800-46 (Eighth Edition, revised February 2003). To facilitate prosecution, however, Applicants have cancelled the non-elected claims without prejudice to or disclaimer of the underlying subject matter.

Applicants also acknowledge the finality of the election requirement to a single nucleotide sequence, but maintain their traversal. This approach contravenes USPTO policy as stipulated in the Manual of Patent Examining Procedure stating that "to further aid the biotechnology industry in protecting its intellectual property without creating an undue burden on the Office, the Commissioner has decided ... to permit a reasonable number of such nucleotide sequences to be claimed in a single application." (MPEP, 8th ed., August 2001, Section 803.04). Applicants submit that no serious burden is created for the Examiner by running a simultaneous computerized search of the disclosed nucleic

acids. The single search may be run in conjunction with databases such as those available at http://www.ncbi.nlm.nih. Therefore, the search of several nucleotide sequences creates no undue burden on the Examiner, whereas, the restriction to a single nucleotide sequence, by contrast, imposes a serious burden on the Applicants. Moreover, Applicants reiterate that SEQ ID NOs: 3 to 463 are partial subsequences of SEQ ID NO: 1 and that no undue burden would be placed upon the Examiner by examining SEQ ID NO: 1 together with SEQ ID NOs: 3 to 463. However, in order to facilitate prosecution Applicants have removed non-elected sequences from the claims without prejudice to or disclaimer of the underlying subject matter.

B. Information Disclosure Statement

Applicants thank the Examiner for returning signed copies of the Form 1449 for the information disclosure statements filed on March 6, 2002.

C. Claim Objections

Claims 24, 34, and 39 have been objected to on the grounds that "[t]hese claims do not have an elected nucleic acid sequence from SEQ ID NO: 3 through 463." Office Action at page 2. In order to facilitate prosecution, and without acquiescing to the Examiner's imposition of an election of species requirement, Applicants have cancelled claims 24, 34, and 39 without prejudice to or disclaimer of the underlying subject matter. For at least the foregoing reasons, Applicants submit that the objections to claims 24, 34, and 39 have been rendered moot. Applicants therefore respectfully request that the claim objections be withdrawn.

D. Rejections under 35 U.S.C. § 112, first paragraph (Written Description)

Claims 22-40 stand rejected under 35 U.S.C. § 112, first paragraph as allegedly containing subject matter which was not described in the specification in such as way as

to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Office Action at page 3. The Office alleges that "[a]ll of the current claims encompass a genus of nucleic acids, which is a polymorphism in a promoter region of the optineurin gene," and further alleges that this genus is not fully disclosed in the specification. Rather, the Office asserts that "[t]his large genus is represented in the specification by only the polymorphisms listed in Table 1." Office Action at page 3. The Office also alleges that there are "[n]o structural limitations or requirements which provide guidance on the identification of sequences which meet the functional limitations of associating a polymorphism for diagnosing glaucoma by detecting a polymorphism in a promoter region of the optineurin gene." Office Action at page 4. Applicants disagree.

An adequate written description of a genus of nucleic acids may be achieved by means of a "recitation of a representative number of [members], ...or of a recitation of structural features common to the members of the genus." *Regents of the University of California v. Eli Lilly and Co.*, 119 F.3d 1559, 1568-69, 43 U.S.P.Q.2d 1398, 1406 (Fed. Cir. 1997). Moreover, the written description requirement can be met by "show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics...*i.e.*, complete or partial structure, other physical and or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics." *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 323 F.3d 956, 964 (Fed. Cir. 2002). (quoting from Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, 66 Fed. Reg. 1099, 1106 (Jan. 5, 2001)).

Applicants respectfully submit that the instant specification complies with the written description requirement. Applicants thank the Examiner for acknowledging that Applicants "have express possession of" the eighteen polymorphisms listed in Table 1. *See, e.g.*, Office Action at page 4. Applicants also note that the instant specification provides the complete nucleotide sequence of SEQ ID NO: 1. Applicants respectfully submit that the polymorphisms listed in Table 1 provide a recitation of a representative number of members of the genus set forth in claims 22-40. Moreover, in combination

with the complete nucleotide sequence of SEQ ID NO: 1, the polymorphisms listed in Table 1 reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

For at least the foregoing reasons, Applicants submit that the written description rejections under 35 U.S.C. § 112, first paragraph, have been overcome or rendered moot. Applicants therefore respectfully request that the written description rejections be withdrawn.

E. Rejections under 35 U.S.C. § 112, first paragraph (Enablement)

Claims 22-40 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter that was not described in the specification in such as way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention without undue experimentation. Office Action at page 4. The Office alleges that "given the broad claims in an art whose nature is identified as unpredictable, the unpredictability of that art, the large quantity of research required to define these unpredictable variables, the lack of guidance provided in the specification, the absence of any working examples, and the negative teachings in the prior art balanced only against the high skill level in the art, it is the position of the examiner that it would require undue experimentation for one of skill in the art to perform the method of the claim as broadly written." Office Action at page 7. Applicants respectfully disagree.

It is well-established law that "the enablement requirement is met if the description enables any mode of making and using the invention." *Johns Hopkins University v. CellPro*, 152 F.3d 1342, 1361, 47 U.S.P.Q.2d 1705, 1719 (Fed. Cir. 1998) (emphasis added), *quoting Engel Indus. v. Lockformer Co.*, 946 F.2d 1528, 1533, 20 U.S.P.Q.2d 1300, 1304 (Fed. Cir. 1991). Because Applicants need only establish a single mode of making and using the invention, and have done so in this case, Applicants have enabled the claimed invention.

Moreover, contrary to the Office's assertions, an *In re Wands* analysis also supports Applicants' position that no undue experimentation would be required to make and use the claimed invention. *In re Wands*, 858 F.2d 731, 737, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1998). The first *Wands* criterion is the quantity of experimentation necessary. The "make-and-test" quantum of experimentation is reduced by the extensive knowledge, for example of the methods for identifying and screening for polymorphisms and of the nucleotide sequence of SEQ ID NO: 1, to which a person of ordinary skill in the art has access. *See, e.g.*, specification at pages 106-112, Example 1 and Table 4. Performing routine and well-known steps cannot create undue experimentation even if it is laborious. *In re Angstadt*, 537 F.2d 498, 504, 190 U.S.P.Q. 214, 218-219 (C.C.P.A. 1976).

The Office Action appears to express concern that testing of the putative positives would entail screening through some false positives. Office Action at page 6. This concern is misplaced. "It is not a function of the claims to specifically exclude...possible inoperative substances." *Atlas Powder Co. v. E. I. du Pont de Nemours & Co.*, 750 F.2d 1569, 1576, 224 U.S.P.Q. 409, 413 (Fed. Cir. 1984) (citing *In re Dinh-Nguyen*, 492 F.2d 856, 858-59, 181 U.S.P.Q 46, 48 (C.C.P.A. 1974)). The case law does not require "each and every compound within a claim to be equally useful for each and every contemplated application." *Ex Parte Cole*, 223 U.S.P.Q. 94, 95 (B.P.A.I. 1983).

The second Wands criterion is the amount of direction or guidance given in the specification. Applicants respectfully submit that the specification provides ample guidance, by describing various types of makers (*see, e.g.*, specification at page 103, line 19 through page 106, line 12) and various methods for using a marker nucleic acid molecule to identify a polymorphism and to diagnose glaucoma (*see, e.g.*, specification at page 106, line 12 through page 111, line 8; Example 1; and Table 4). In addition, the specification describes general features of nucleic acid probe hybridization and the selection of PCR primers (*see, e.g.*, specification at page 48, line 12 through page 53, line 6); and provides reference to a number of texts describing basic molecular biology techniques (*see, e.g.*, specification at page 14, lines 19 through page 15, line 9).

The third Wands criterion is the presence or absence of working examples. Applicants thank the Examiner for acknowledging that "[t]he specification has a working example of the identification of SNPs in the optineurin promoter." Office Action at page 6. The Office further alleges, however, that "the method does not apply the marker nucleic acid molecule having a nucleic acid sequence that specifically hybridizes to a sequence selected from the group consisting of SEQ ID NO: 1 and a complement thereof and a complementary nucleic acid molecule obtained from a sample." Office Action at pages 6-7. Applicants respectfully disagree. For example, in Example 1, polymerase chain reaction (PCR) and DNA sequencing are used to identify polymorphisms in the optineurin promoter. Standard PCR and DNA sequencing methods involve the use of primer (*e.g.*,marker) nucleic acid sequences; applying these methods to sequences within the optineurin promoter would involve the use of marker nucleic acid sequences within the optineurin promoter. *See, e.g.,* specification at page 111, line 10 through page 112. The specification also provides that in a preferred embodiment, "the marker is capable of acting as a PCR primer" (*see, e.g,* specification at page 104, lines 6-9), and that SNPs may be characterized by direct or indirect sequencing of the site. *See, e.g.,* specification at page 108, lines 3-4. For at least these reasons, Applicants respectfully disagree that the specification fails to provide a working example of the invention.

The fourth criterion focuses on the nature of the invention. The claims recite, for example, "[a] method for diagnosing glaucoma in a sample obtained from a cell or a bodily fluid by detecting a polymorphism in a promoter region of the optineurin gene...". Practitioners in the art, therefore, are guided not only by the specification itself but also by considerable knowledge and numerous resources regarding conditions and approaches that can be utilized to identify and screen polymorphisms. As noted above, many resources, such as Maniatis' *Molecular Cloning: A Laboratory Manual*, are readily available to the skilled art worker. *See, e.g.,* specification at pages 14, lines 19 through page 15, line 9. Such resources, together with the specification and the art worker's own knowledge, provide ample guidance so that one of ordinary skill in the art is readily enabled to make and use the claimed invention.

The fifth, sixth, and seventh criteria focus on the state of the art, the relative skill in the art, and the predictability of the art, respectively. The Office acknowledges that the level of skill in the art is high. Office Action at page 7. But the Office appears to assert that a reference by Rezaie *et al.* supports a high level of unpredictability in the art of the present invention. *See, e.g.,* Office Action at page 7. Applicants respectfully disagree. Applicants note that the teaching of Rezaie *et al.* is not directed to a method for diagnosing glaucoma in a sample obtained from a cell or a bodily fluid by detecting a polymorphism in a promoter region of the optineurin gene. As such, reliance by the Examiner is misplaced. Moreover, Applicants note that even though some optineurin mutations may not be predictive of glaucoma, it is well-established that it is not a function of the claims to specifically exclude possible inoperative substances. *Atlas Powder*, 750 F.2d at 1576, (Fed. Cir. 1984).

The eighth criterion focuses on the breadth of the claims. Enablement is satisfied when the disclosure "adequately guide[s] the art worker to determine, without undue experimentation, which species among all those encompassed by the claimed genus possess the disclosed utility". *See In re Vaeck,* 947 F.2d 488, 496, 20 U.S.P.Q.2d 1438, 1445 (Fed. Cir. 1991). Here, enablement is satisfied because the art worker is specifically guided by the disclosure to look, for example, to the sequence of SEQ ID NO: 1 and various standard methods for screening for polymorphisms, in making that determination.

Accordingly, based on the foregoing, the enablement rejection under 35 U.S.C. § 112, first paragraph, is incorrect and should be withdrawn. Applicants therefore respectfully request that the enablement rejections be withdrawn.

F. Rejections under 35 U.S.C. § 112, second paragraph (Claim indefiniteness)

Claims 22-40 stand rejected under 35 U.S.C. § 112, second paragraph for claim indefiniteness on the grounds claims 1, 32, and 40 recite "a complementary nucleic acid molecule obtained from a sample." The Office alleges that it is unclear whether or not the complementary nucleic acid molecule from a sample is complementary to the marker nucleic acid molecule. Applicants disagree.

The test for determining whether terms in a given claim are indefinite is whether one skilled in the art would understand what is claimed. *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 927 F.2d 1200, 18 U.S.P.Q.2d 1016 (Fed. Cir. 1991), *cert denied,* 112 S.Ct. 169 (1991). M.P.E.P. § 2173.02 states that "[d]efiniteness of claim language must be analyzed, not in a vacuum, but in light of: (A) The content of the particular application disclosure; (B) The teachings of the prior art; and (C) The claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made."

Applicants respectfully submit that claims 22-40 are not indefinite in the recitation of "a complementary nucleic acid obtained from a sample." For example, clause (B) of claim 22 recites "permitting hybridization between said marker nucleic acid molecule and said complementary nucleic acid molecule." Applicants submit that a person of ordinary skill in the art reading claim 22 in its entirety and in light of their knowledge of the art would understand (for example, on the basis of clause (B)) that the marker nucleic acid is complementary to said complementary nucleic acid obtained from a sample. Applicants also point out that independent claims 32 and 36 also recite a clause (B) having the same language as clause (B) of claim 22.

Applicant therefore submits that the grounds for the indefiniteness rejections of Claim 22-40 have been obviated or rendered moot. In light of these remarks, Applicants respectfully request withdrawal of these rejections.

CONCLUSION

In view of the above, each of the presently pending claims is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to pass this application to issue. The Examiner is encouraged to contact the undersigned at 202.942.5512 should any additional information be necessary for allowance.

Respectfully submitted,

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